

## RESEARCH ETHICS

## Sham surgery controls are mitigated trolleys

R L Albin

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Debate continues about the ethics of sham surgery controls. The most powerful argument for sham surgery controls is that rigorous experiments are needed to demonstrate safety and efficacy of surgical procedures. Without such experiments, there is danger of adopting worthless procedures in clinical practice. Opponents of sham surgery controls argue that sham surgery constitutes unacceptable violation of the rights of research subjects. Recent philosophical discussion has used two thought experiments—the transplant case and the trolley problem—to explore the circumstances under which individuals may be harmed to benefit a larger group. The transplant case is felt to exemplify circumstances that forbid harming some to benefit a larger group while the trolley problem exemplifies circumstances that permit harming some to benefit others. I argue that sham surgery controls satisfy criteria derived from the trolley problem and are morally permissible.

Sham surgery controls (surgical placebos) are rarely used components of human clinical research.<sup>1–6</sup> Debate about the acceptability of sham surgery controls in human studies was triggered recently by the employment of sham surgeries in studies of fetal mesencephalic tissue grafts for Parkinson's disease.<sup>7–8</sup> In conventional medical placebo controlled trials, the placebo is inactive. Control research subjects forgo the hoped for benefits of the experimental treatment but are presumed not to incur any additional risks from the placebo treatment. In trials with sham surgery controls, the control subjects will not receive any possible benefit from the experimental intervention but are exposed to risks associated with the experimental procedure.

## SHAM SURGERY CONTROLS: HISTORY AND CONTROVERSY

Critics of sham surgery control designs argue that this difference constitutes an intolerable infringement of the rights of research subjects.<sup>8–12</sup> These critics, however, do not generally address the most powerful argument in favour of sham surgery controls; that use of surgical placebos is necessary for the rigorous experimental designs needed to exclude false positive trial results.<sup>7–13–15</sup> False positive trial results could admit into routine clinical practice procedures with little or no benefit and significant risk for patients. The history of sham surgery controls supports the

view that sham surgery controls prevent false positive trial results.

The pioneering sham surgery studies were a pair of small randomised trials of internal mammary artery ligation for angina.<sup>1,2</sup> These trials demonstrated no specific benefit of internal mammary artery ligation at the time when this procedure was used in clinical practice. The experiments, which involved a handful of research subjects, prevented thousands of individuals from being exposed to needless risks. Moseley *et al* reported recently a sham controlled study of the effect of arthroscopic debridement or lavage of the knee joint as treatment for osteoarthritis pain.<sup>3</sup> Efficacy of this procedure has been suggested by non-placebo controlled studies, but no benefit was shown in this study. Arthroscopic debridement and/or lavage for osteoarthritic knee pain has been a routine procedure applied to tens of thousands of patients annually in the USA at a cost of hundreds of millions of dollars. While arthroscopy is a safe procedure, it is not risk free and is often done under general anaesthesia. Efforts were made in the study to minimise the risk of the procedure in sham surgery subjects. The sham procedure omitted general anaesthesia and superficial skin incisions were made to mimic arthroscopy. No instrument was placed in the joint.

In two Parkinson's disease grafting trials, evidence was found of significant placebo effects that would have not have been detected in self control (patient preoperative status) or parallel medical treatment design studies.<sup>6–16</sup> Efforts were made to design a sham surgery procedure that minimised the major risks of the procedures. The utility of sham surgery controls is unmistakable.

Critics of sham surgery control designs also argue that the problem of placebo effects is overblown. This argument is based largely on a meta-analysis of placebo effects published by Hrobjartsson and Gotzsche.<sup>17</sup> The conclusions of this study, however, are more nuanced than acknowledged by sham surgery critics. Hrobjartsson and Gotzsche report the existence of significant placebo effects in at least two important situations. Substantial placebo effects were found in studies of pain interventions and also in studies where the primary outcome variable was a subjective and continuously varying measure. Concerns about placebo effects are legitimate in studies of pain interventions, as shown in the internal mammary artery ligation and knee osteoarthritis studies. Many studies, including the Parkinson's disease grafting studies, employ subjective and continuously varying outcome measures. There is evidence also that procedures have a larger placebo effects medical placebos.<sup>18</sup> Placebos are important not only for

Correspondence to:  
Dr R L Albin, 4412D  
Kresge III, 200 Zina Pitcher  
Place, Ann Arbor, MI,  
48109-0585, USA;  
ralbin@umich.edu

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guarding against the placebo effect per se but are also safeguards against other forms of bias, such as investigator bias.<sup>17</sup>

Given the utility of sham surgery controls, the question of whether these controls are an unacceptable violation of the rights of research subjects is crucial. If important rights of research subjects are violated, sham surgery controls are forbidden. Determining the moral permissibility of sham surgery controls is an example of attempting to determine if benefits for many justify increased risks for a few. Philosophical discussion about imposing risks on a few to benefit a larger number has focused on a pair of thought experiments, the transplant case and the trolley problem.<sup>19–21</sup> These cases exemplify contrasting situations in which a few either cannot be put at risk to benefit others or risks to the few are morally permissible. Discussion of these and related thought experiments led to the proposed criteria for determining if actions in which some are placed at risk of harms to benefit many are morally permissible. This discussion provides guidance for evaluating the moral acceptability of sham surgery controls.

### TRANSPLANT AND TROLLEY

The transplant case and the trolley problem are used to examine moral intuitions about the circumstances in which a few may be put at risk to benefit others. The hope is that this examination will make the basis for moral intuitions explicit. By examining the differences between these two thought experiments, philosophers have attempted to isolate the key factors that permit putting a few at risk to benefit others and perhaps allow specification of criteria for moral guidance. These thought experiments are formulated as stark, even extreme, scenarios involving life saving interventions for several and death for one. By examining the problem of putting a few at risk to benefit many with these stark thought experiments, some moral philosophers have attempted to determine the outer limits of moral permissibility for putting a few at risk to benefit many in the setting of relatively conventional moral intuitions.

In the transplant case, a surgeon has five patients whose death is imminent without organ transplantation, but different organs are affected in the different patients. The surgeon suddenly encounters a person who is a perfect donor for all five affected patients. The surgeon proceeds to operate on and kill the perfect donor and save the five patients. One has died to save five but moral intuition indicates that the surgeon's actions are impermissible. In the trolley problem, a runaway trolley is proceeding down a track towards five workmen who will be killed if the trolley is not stopped or diverted. The trolley's brakes are not operative but there is an opportunity to divert the trolley onto a branch track. On the branch track, however, is a single workman who will be killed if the trolley is diverted. The diversion can be made by either the trolley driver (the original trolley problem) or a bystander (bystander at the switch trolley problem). Regardless of whether the driver or the bystander diverts the trolley, the result is kill one to save five. Moral intuition indicates that this action is permissible, though not obligatory. Introduced originally by Philippa Foot to address other concerns, and explored in the present context by Judith Thomson, the trolley problem exemplifies an unusual circumstance in which harming or placing some at risk to benefit a larger group is legitimate.<sup>19</sup> Some philosophers have expended considerable ingenuity not only in contrasting transplant and trolley but also in constructing variants of both thought experiments in efforts to isolate key differences between these two situations.<sup>19–21</sup> In turn, identification of the features that make the diversion of the trolley morally permissible allow specification of criteria for evaluating when putting some at risk to benefit others is morally permissible. Thomson presented two major analyses identifying key

features governing the moral permissibility of trolley-like behaviour.<sup>19–21</sup> The second of these analyses is not only more convincing but also yields criteria that can be applied more easily to real problems.<sup>19–21</sup> These are not, however, the only formulations of criteria derived from transplant-trolley. Kamm developed an alternative analysis.<sup>20</sup> Because I find Kamm's analysis less convincing and harder to apply to real problems, I will restrict discussion to Thomson's analyses.

In her original analysis, Thomson suggested two key features differentiate trolley from transplant.<sup>19</sup> First, in trolley, an existing threat is diverted from the five to the one whereas in transplant, the threat to the one is wholly novel and created by the surgeon. Thomson explores variants of trolley and some related thought experiments. Thought experiments where it is morally permissible to divert risk from many to one have in common the feature that the agent diverting risk from many to one "minimizes the number of deaths which get caused by something that already threatens people, and that will cause deaths whatever the bystander does". Thomson refers to this as the "distributive exemption". The second key condition Thomson specifies for allowing risk to be diverted from many to one is that diversion of risk from many to one is acceptable if the means by which the diversion is accomplished does not constitute an unacceptable infringement of the rights of the one. To explore this issue, Thomson contrasted the original trolley problem with a variant called fat man. In this version of trolley, the bystander is not at a switch capable of diverting the trolley but standing next to an additional and obese bystander. If the bystander (the same argument applies to the trolley driver and an obese passenger in the trolley) pushes the obese bystander into the path of the trolley, the trolley stops. This action saves the five workmen, but the obese bystander is killed. Thomson points out correctly that moral intuition indicates that pushing the obese bystander into the path of the trolley is morally impermissible. Thomson suggests that the key difference between the original trolley experiment and fat man is that in the fat man, the agent bystander has violated a "stringent right" of the one, presumably the right not to be killed, and such a violation has not taken place in the original trolley scenario. This is plausible but also arguable. Certainly, diversion of the trolley onto the branch track results in death no less than throwing the obese bystander onto the track. Death of the one ensues from an act of the bystander (or driver). How has a stringent right violation not occurred in trolley? Thomson's analysis does not make this perfectly clear. One possible, but debatable option, would be to invoke the difference between killing and letting die, but given the controversy over differentiating killing and letting die, this will not provide a clear solution.

Generalising Thomson's first analysis of transplant, trolley, and other thought experiments, we can identify two criteria for determining when it is morally permissible to putting some at risk for increased harm to shield a larger number from that risk.

- The risk of harm must exist previously and that risk of harm will occur regardless of what the agent (driver, bystander) does. This is the "distributive exemption".
- The agent's action of harm diversion does not violate some stringent right of the few.

One difficulty with these criteria is that it is not immediately obvious why diversion of an existing harm is different from creation of a new harm. For the worker on the branch track, it could be argued that diversion of the trolley constitutes a novel harm. Another difficulty is that definition of the nature of "stringent rights" is not specified or intuitively obvious. Finally, it is uncertain how to determine

if a proposed action of harm diversion constitutes a rights violation. This last point makes these criteria difficult to apply in practice. They fail to capture completely what makes the behaviour of the agent (driver, bystander) in trolley morally permissible.

In later work examining the general nature of rights, Thomson presents a modified and more restrictive formulation of trolley.<sup>21</sup> She rejects her earlier conclusion regarding the simple “distributive exemption” and constructs a trolley variant in which the five on the main track are not workers but “thrillseekers” who have illegally placed themselves on the track and made wagers on whether or not the trolley (which they don’t know is a runaway trolley) can stop before reaching their position. The one is a trolley company employee who has been assured that the branch track will not be used. The driver and bystander are aware of the identities and situations of both the five and the one. In this scenario, diverting the trolley from the five to the one is not obviously morally permissible. Thomson then points out a key difference between this variant and the original trolley problem. In the original problem, all the track workers are at risk from trolley accidents as part of their jobs and that risk is essentially the same among workers at the start of the day when they receive their work assignments. Allocation of workers to the main track (the five) or to the branch track (the one) is determined randomly. In the original trolley problem, then, the agent (driver or bystander) is not just diverting a pre-existing harm from the five to one but is focusing a pre-existing harm that originally threatened all track workers from a larger subset of track workers (the five) to a smaller subset of track workers (the one). To generalise and provide explicit criteria, harming a few to save many is acceptable when: (a) specific group is at risk from a harm causing event(s); (b) the setting in which the harms (or risks) are diverted from the many to the few involves only individuals drawn from the larger at risk group; (c) harm (or risk) is diverted/focused between larger and smaller subsets of the originally at risk group, or the diversion/focus occurs between the entirety of the originally at risk group and a subset of the group; and (d) harm (or risk) will occur regardless of whether or not the agent diverts/focuses the harm (or risk) from the many to the few.

These criteria restrict the scope significantly of circumstances in which putting some at risk to benefit others is morally permissible. They preserve the concept of a pre-existing threat but both the many and the few must be threatened with the harm (or risks) prior to the situation in which harm (or risk) is diverted from the many to the few. This avoids the issue of assessing threat novelty that bedeviled the first criterion in Thomson’s original analysis.

Thomson’s stipulation that the track workmen in trolley are randomly allocated to either the main track or the branch track implicitly points out another important criterion. In legitimising diversion of harm (risk) from the many to the few there must be some fair and legitimate process for allocating the risk from the many to the few. If it were known that trolley brakes had a high probability of failure on the stretch of track leading to the branch between the main track and the branch in the trolley problem, and workers were non-randomly allocated between the main track and the branch, then the moral permissibility of the agent (driver or bystander) diverting the trolley from the main track to the branch is less obvious. In Thomson’s restrictive reformulation of trolley, the risk allocation process that participates in legitimising diversion of harm from the many to the few is random assignment of workers to either the main track or its branch. Other reasonable processes, which are not based on random or even equitable risk allocation, can be legitimate. For example, one real, socially accepted, and clearly morally

permissible situation in which risk is diverted from many to few is selection of combat personnel during wartime. In a war, all personnel in the armed forces are nominally exposed to risks associated with combatant status. The risk of harm, however, is disproportionate for those serving in combat units. Assignment to combat units does not involve random allocation from the whole population of armed service personnel but rather compulsory assignment of those likely to perform best. Generalising Thomson’s implicit point about allocation of risk indicates another criterion for determining when harming a few to benefit many is legitimate: (e) there is a reasonable and legitimate means for allocating risk between the few and the many.

## SHAM SURGERY CONTROLS AND TROLLEY CRITERIA

It is reasonable to ask how the trolley problem is analogous to the use of sham surgery controls. The analogy is not between the trolley model and a given clinical trial but rather between trolley and the general problem of determining if sham surgery controls are morally permissible in any scientifically reasonable design. The trolley derived criteria can be used to evaluate the moral permissibility of sham surgery controls in general. Sham surgery controls satisfy the criteria derived from Thomson’s restrictive analysis of trolley. Novel (or presently used but inadequately evaluated) surgical interventions are a threat to all patients in whom they could be applied, satisfying criterion (a). Experiments involving sham surgery controls involve only subjects with the medical condition in question, satisfying criterion (b). Sham surgery controls are employed in a subset of the patient populations that would be (for novel procedures—for example, fetal tissue engraftment for Parkinson’s disease) or are (procedures already in clinical practice—for example, knee arthroscopy for osteoarthritis pain) candidates for the surgical procedure, satisfying criterion (c). Harm (or risk) occurs regardless of whether the sham surgery controlled experiment is performed, because the surgical procedure will be (or is, in the case of presently used interventions) implemented in clinical practice unless a good experiment undermines its efficacy, satisfying criterion (d). Criterion (e) is satisfied by enrolment in a properly designed and executed trial following accepted scientific and ethical standards for clinical research. Examination of sham surgery controls in the light of transplant and trolley demonstrates that sham surgery controls are morally permissible.

## SHAM SURGERY CONTROLS AS MITIGATED TROLLEYS

The use of sham surgery controls, such as recently in fetal tissue engraftment for Parkinson’s tissue and the study of treating knee osteoarthritis pain satisfies not only the trolley derived criteria but deviates from the trolley model in a way that provides further mitigation of moral discomfort related to use of sham surgery controls. By using the criteria derived from Thomson’s restrictive formulation of trolley we would be justified in performing the complete sham analogue of the surgery in control subjects. In the fetal tissue engraftment and arthroscopy trials, the sham procedures were designed to minimise the major risks associated with the surgeries. Guidelines for experiments containing sham surgery controls specify that every effort be made to reduce risks to the sham surgery control groups. It is important to recognise that these efforts do not and cannot reduce the risk to zero. In the Parkinson’s disease fetal engraftment experiments, sham subjects received a stereotaxic frame, some medications for surgery, spent hours in the operating room without the benefit of their Parkinson’s medication, and had an outer table burr hole. In the knee osteoarthritis study, major risks



were avoided completely but rare complications like an unexpected anaphylactic reaction to an administered medication are impossible to prevent. These efforts to reduce risk for the controls, nonetheless, have real moral value. Intuition suggests that risk reduction efforts for the controls increase the moral acceptability of sham surgery controls. For example, a common example of exposing some to increased risk to benefit many is the employment of firefighters. One of the factors that legitimises employment of dedicated firefighters is that they receive special training and equipment. Without this form of risk mitigation, it would be hard to argue that employment of firefighters is morally permissible. Returning to the trolley scenario, risk reduction for sham surgery controls is akin to diverting the trolley from the main track to the branch while simultaneously placing padding on the front of the trolley in an effort to cushion the impact of the trolley. Sham surgery controls are a kind of trolley in which the risks to the one are mitigated.

## THE ROLE OF CONSENT

The usefulness of the transplant/trolley examination and the criteria derived from this examination are illustrated further by using them to examine the role of consent in legitimising sham surgery controls. It would be morally impossible to perform these kinds of experiments without informed consent, but some proponents of sham surgery controls have argued that informed consent is the crucial, implicitly necessary, and sufficient factor that permits the use of sham surgery controls. Freeman *et al.*, for example, place a good deal of weight on informed consent as a moral safeguard in experiments involving sham surgery controls.<sup>7</sup> Similarly, Bernat suggested that sham surgery controls are acceptable after informed consent because participation allows patients to make “an ennobling gesture of volunteerism to use their illness to contribute to research that may improve the lives of future patients”.<sup>22</sup> Consent, however, is a difficult defence for sham surgery controls. The well known “therapeutic misconception” describes the phenomenon of subjects of clinical trials tending to assume that the intervention offered has therapeutic value. The prevalence of this phenomenon undermines the idea that most potential subjects of clinical trials objectively and critically evaluate trial participation.<sup>23</sup> Informed consent is necessary but cannot be the necessary and sufficient factor legitimising the use of sham surgery controls.

Examination of the possible role of consent in transplant/trolley clarifies the role of consent in employment of sham surgery controls. In transplant, even if the one gave informed consent and was considered competent, the surgeon’s action would still be impermissible. In trolley, the one sacrificed for the five does not give consent for diversion of the trolley but diversion of the trolley is still permissible. In these stark scenarios, consent, by itself, does not authorise harming a few to save many. Criterion (e) of the criteria derived from Thomson’s restrictive formulation of trolley, however, specifies the use of a reasonable and legitimate procedure for allocating risk from the many to the few. Informed consent is an indispensable part of almost all acceptable designs for human experimentation (some emergency procedures are an exception) and an indispensable component of the process of legitimately allocating subjects from the larger at-risk population to the sham surgery subgroup. Informed consent is a necessary component of legitimising sham surgery control use, but is not a necessary and sufficient authorisation of sham surgery controls.

## SHAM SURGERY CONTROLS: PERMISSIBLE OR OBLIGATORY

An important aspect of the trolley analysis is that it specifies that harming a few to benefit many is permissible but not

obligatory. Given that sham surgery controls are morally permissible, does that mean that they are required? This question can be answered by examining the alternative of not employing sham surgery controls. Without sham surgery controls, there is demonstrated risk of introducing useless and potentially morbid procedures into clinical practice. This is an intolerable violation of our ethical requirements as physicians and scientists. Without sham surgery controls, the only way to avoid introducing some useless and risky procedures would be to cease research on new and promising interventions, which would also be intolerable. In carefully selected situations, sham surgery controls are permissible and necessary. This is not a blanket justification of sham surgery controls. Sham surgery controls should be used only when absolutely necessary and sham surgery procedures should be designed to minimise risk. Published guidelines for employment of sham surgery controls outline reasonable requirements for use of sham surgery controls.<sup>14 15 24</sup>

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